Exhibit 6

Establishment Inspection Report FEI: **3009298353**
Prinston Pharmaceutical Inc EI Start: 3/29/2016
Cranbury, NJ 08512-3514 EI End: 4/5/2016

TABLE OF CONTENTS

SUMMARY

This Post Marketing Adverse Event (PADE) Inspection of a corporate headquarters was requested by the PADE Compliance Team at the Center for Drug Evaluation and Research (CDER), Office of Compliance per FACTS Assignment ID# 11580984, FACTS Operation ID# 8239467, and MARCS Operation ID# 9231. Guidance for this inspection was provided by Compliance Program 7553.001: Postmarketing Adverse Drug Experience (PADE) Reporting Inspection.

The previous inspection of 11/28/12-11/30/12 was the firm's initial inspection. This inspection provided coverage of the Postmarketing Adverse Event Experience (PADE) reporting for products for which the firm is the applicant holder including: Benazepril Tablets (ANDA 076118); Losartan Tablets (ANDA 091497); and Nevirapine Tablets (ANDA 078644). The inspection also revealed that pharmacovigilance (PVG) activities were contracted out to (b) (4) , (b) (4) . The inspection was classified NAI and no FDA-483, Inspectional Observation was

issued.

The current inspection revealed that Prinston Pharmaceutical, Inc. continues to be the applicant holder of various generic drug products and is responsible for submitting PSUR and 15 Day Alert Reports to the FDA. The firm still contracts out all pharmacovigilance operations to their CRO, (b) (4) (formerly known as (b) (4) This inspection covered the firm's PADE surveillance, receipts, evaluations, processing and reporting system for twenty-six of the firm's drug products.

On 04/05/16, a closeout discussion was held with management regarding the lack of information for ADE reporting after the close of the business day and late reporting of 15 day cases. No FDA-483, Inspectional Observations was issued. No samples were collected and no refusals were encountered.

ADMINISTRATIVE DATA

Inspected firm:	Prinston Pharmaceutical Inc
Location:	2002 Eastpark Blvd Cranbury, NJ 08512-3514
Phone:	609-655-1688
FAX:	609-655-1658
Mailing address:	2002 Eastpark Blvd Cranbury, NJ 08512-3514
Dates of inspection:	3/29/2016-4/1/2016 , 4/4/2016-4/5/2016
Days in the facility:	6
Participants:	**Tonia F Bernard, Investigator** **Zakaria I Ganiyu, Investigator**

Please Note: The inspectional report was written by Investigator Tonia Bernard and Investigator Zakaria Ganiyu.

- "We" refers to both Investigators Bernard (TFB) and Ganiyu (ZIG)
- "I" refers to the investigator identified writing the applicable section.

Investigator Ganiyu was present during the entire inspection except 04/01/2016.

On 03/29/2016, we, investigators Tonia F. Bernard and Zakaria I. Ganiyu, presented our credentials and issued form FDA-482, Notice of Inspection **(Attachment)** to Mr. Hai Wang, Senior Vice President of Business Development and Marketing. Mr. Wang stated that he was the most responsible individual on site at the time of inspection, authorized by Jun Du, Chief Executive Officer of Prinston Pharmaceutical Inc, to accept the Notice. We explained to Mr. Wang that the purpose of our visit was to conduct a PADE inspection of Prinston Pharmaceutical Inc.

HISTORY
ZIG
Prinston Pharmaceutical Inc. (Prinston) was established in 2011, as a spin-off from Huahai US, Inc. based in Cranbury, New Jersey. The firm is headed by Jun Du, Chief Executive Officer/CEO. Prinston is a virtual pharmaceutical firm engaged in the development and commercialization of generic oral drug products that includes, but not limited to: Losartan, Irbesartan, Levetiracetam, Donepezil, etc. Prinston is a subsidiary of Zhejiang Huahai Pharmaceutical Company based in Linhai, Zhejiang, China and Huahai US Inc. based in New Jersey. Zhejiang Huahai manufactures the finished dosed drug products and Prinston markets and distributes in the United States. According to Mr. Wang, Sr. Vice President, Zhejiang Huahai also manufactures for other United States Pharmaceutical firms; (b) (4) Huahai US Inc. is the shareholding company and the holder of the Active Pharmaceutical Ingredients (API) used in the manufacturing and Prinston Pharmaceutical serving as the ANDA holder of these drug products.

In 2012, Prinston acquired Solco Healthcare US (Solco), a marketing and sales organization based in the same Cranbury, NJ office building as Prinston. Solco serves as the sales and distribution entity of Prinston. All Prinston's (ANDA holder) drug products are labeled as "Distributed by Solco® Healthcare U.S." except Losartan by Rising Pharmaceuticals, Allendale, NJ and Nevirapine by Breckendridge Pharmaceuticals, Boca Raton, FL.

Prinston Pharmaceutical occupies a 3-unit Cranbury, NJ office building; two of which are occupied by Prinston/Huahai US and the other office space dedicated to Solco Healthcare U.S. The entire space is approximately (b) (4) sq. ft. with (b) (4) Prinston and (b) (4) Solco employees. The firm operates between the hours of (b) (4) as needed. According to Mr. Hai Wang, Senior VP, Business Development and Sales, Prinston's 2015 sales revenue were approximately (b) (4) .

Post-inspectional correspondence should be addressed to:
Jun Du, CEO
Prinston Pharmaceutical Inc.
2002 EastPark Blvd
Cranbury, New Jersey 08512

INTERSTATE COMMERCE
ZIG
According to Mr. Wang, Prinston is completely a virtual pharmaceutical firm that operates 100% interstate and 100% wholesale. All Prinston /Solco marketed oral drugs are distributed throughout the United States.

Prinston's Top 5 Major Distributors/Customers:

(b) (4)

JURISDICTION
ZIG
Prinston Pharmaceutical's currently marketed oral drug products and ADE responsibilities:(Exhibit 1)

Drug Product	ANDA Holder	Distributed By	ANDA #	ADE Reporting Responsibility
Benazepril HCl	Prinston	Solco	A076118	Prinston
Bupropion SR	Prinston	Solco	A202304	Prinston
Donepezil HCl	Prinston	Solco	A200292	Prinston
Irbesartan	Prinston	Solco	A203071	Prinston
Irbesartan HCTZ	Prinston	Solco	A203072	Prinston
Levetiracetam	Prinston	Solco	A078106	Prinston
Levetiracetam ER	Prinston	Solco	A203468	Prinston
Lisinopril (2.5mg-10mg)	Prinston	Solco	A076180	Prinston
Lisinopril (20mg-40mg)	Prinston	Solco	A076164	Prinston
Losartan	Prinston	Solco/Rising*	A091497	Prinston/Rising*
Methocarbomol (500mg)	Prinston	Solco	A086989	Prinston
Methocarbomol (750mg)	Prinston	Solco	A086988	Prinston
Paroxetine	Prinston	Solco	A203854	Prinston
Risperidone	Prinston	Solco	A077493	Prinston
Ropinirole HCl	Prinston	Solco	A078110	Prinston
Valsartan	Prinston	Solco	A204821	Prinston
Nevirapine	Prinston	Breckenridge	A078644	Prinston
Valsartan /HCTZ**	Prinston	Solco	A206083	Prinston
(b) (4)		Solco	(b) (4)	
(b) (4)	(b) (4)	Solco	(b) (4)	(b) (4)

(b) (4)		Solco	(b) (4)	(b) (4)
(b) (4)	(b) (4)	Solco	(b) (4)	(b) (4)
(b) (4))	(b) (4)	Solco	(b) (4)	(b) (4)
(b) (4) (600mg, 800mg)	(b) (4)	Solco	(b) (4)	Prinston
(b) (4)	(b) (4)	Solco	(b) (4)	Prinston
(b) (4)	(b) (4)	Solco	A203769	(b) (4)

Please Note: All of the above drug products are manufactured by Zhejiang Huahai Pharmaceutical in China.

*****Rising Pharmaceuticals (Rising) has a license agreement with Prinston Pharmaceutical to market and distribute the same ANDA *Losartan* drug as distributed by Solco. In the Master Services Agreement between the two firms we reviewed, Rising is responsible for intake/receipt and evaluation of ADE cases (via (b) (4) and Prinston is responsible for submitting the cases to the Agency.

******Valsartan/HCTZ was recently approved by the FDA (2/08/2016) and has not been marketed at the time of inspection.

INDIVIDUAL RESPONSIBILITY AND PERSONS INTERVIEWED
ZIG
The following management personnel were present during the close-out of the inspection. Please refer to **(EXHIBIT 2)** for a copy of the firm's organizational chart.

- **Jun Du, CEO** is the head of Prinston Pharmaceutical, Cranbury, NJ. Mr. Du oversees all the strategic, business and operational aspects of the organization; R&D, Regulatory Affairs, Quality, Business Development, and Sales & Marketing. Mr. Du was present on the second day through the close-out of the inspection and assisted in answering some ADE inspectional questions.

- **Hai Wang, Senior Vice President of Business Development and Marketing** is responsible for business development activities, strategic partnership, corporate strategy development and planning, product internal and external-licensing, sales and marketing. On 3/29/2016, Mr. Wang accepted the form FDA-482, Notice of Inspection and stated that he was authorized by Mr. Jun Du, CEO, to accept the Notice. Mr. Wang was present from the initial day of the inspection through the close-out of the inspection on 4/05/2016. He provided a PowerPoint presentation overview of the firm's history and assisted in providing us documents and answering ADE related questions. Mr. Wang reports to Mr. Du, CEO.

- **Wei (Helena) Tong, PhD, Senior Director of Regulatory Affairs** is in charge of the overall operations of the Regulatory and Scientific Affairs of Prinston Pharmaceutical. Some of Dr. Tong's responsibilities at Prinston includes, but not limited to: preparation and submissions of regulatory reports (ADE, ANDA, etc) to the Agency, supervising pharmacovigilance related activities, maintaining communication with CROs to ensure regulatory documentations are current and compliant with the Agency. Dr. Tong facilitated and provided us with all requested documents. She also answered our questions and maintained communication with the firm's CRO, (b) (4) for requests of ADE documentations. Dr. Tong was present from the initial day of the inspection through the close-out on 4/05/2016. Dr. Tong reports to Dr. Xiaodi Gu, Executive Vice President of R&D, who reports to Mr. Du, CEO. He was not present during the inspection. Dr. Xiaodi also maintains an office at 2002 Eastpark Blvd, Cranbury, NJ.

- **Remonda Gergis, Senior Director of Quality Assurance** is responsible for auditing the firm's CROs, establishing SOPs, conducting cGMP training for all personnel, reviewing and approving quality investigations, deviations, OOS, complaints, etc. Ms. Gergis was present throughout the inspection and assisted in providing us ADE inspectional documents. She reports to Mr. Du, CEO.

- (b) (6) (b) (6) **Regulatory Affair Associate** works alongside Dr. Tong to perform pharmacovigilance activities. She is responsible for preparing and submitting 15-Day Alert and PSUR ADEs reports to the FDA. Ms. (b) (6) was present throughout the inspection and assisted in providing ADE related documents. Ms. (b) (6) reports to Dr. Tong.

FIRM'S TRAINING PROGRAM
TFB

During the inspection, I reviewed Prinston Pharmaceutical employee training records. The firm's training program consists of training in company functional areas and job specific training. Employees within the Regulatory Affairs Department are trained on SOPs applicable to their job function and are required to re-train whenever a procedure is updated. General training procedures are outlined in Prinston Pharmaceutical's SOP # PRN-3007 "Employee Training" (Effective Date: 06/20/2014). I reviewed SOP and ADE training records for Senior Director of Regulatory Affairs and Regulatory Affair Associate. No deficiencies were noted during the review of Prinston Pharmaceutical training documentation

MANUFACTURING/DESIGN OPERATIONS

Manufacturing/Design Operations
TFB

Adverse Drug Event (ADE) Reporting

According to Dr. Tong, Senior Director of Regulatory Affairs, adverse events are handled by the firm's CRO, (b) (4) (formerly (b) (4)). The following is a brief overview of operation performed at (b) (4) by PVG staff for spontaneous case reporting.

- Incoming AE's are received by a Pharmacovigilance Management Staff specialist via telephone, mail or fax, where the following information is collected and completed within (b) (4) day during the initial intake process: contact information from reporter, patient information, product name, strength lot number, expiration date.

- Medical review by a physician will review the cases to determine the following: case narrative, event terms, coding, seriousness and expectedness of the report.

- 15- Day Alert Cases are sent to Prinston by the (b) (4) day for regulatory review and submission to the Agency within 15 days via mail/E2B submission.

- Each quarterly Periodic Safety Update Report (PSUR) is sent to Prinston within (b) (4) days following the end of the reporting period and each yearly PSUR is sent within (b) (4) days of the following end date of the reporting period, with submission to agency by their respective due date.

I asked Dr. Tong for all of the PVG procedures from their CRO, (b) (4) She supplied me with the following procedures.

- (b) (4) / **Prinston Pharmaceutical, Inc. Client Protocol**

  This protocol outlines the operational process and responsibilities associated with the services provided by (b) (4) for Prinston. During the review, we notice that the protocol lacked information regarding hours of operation at the close of business day for ADE reporting, which is noted under General Discussion with Management section of this report.

- **SOP 01-PR-006 NDA, ANDA, BLA, DESI, Marketed Health Products and Medicinal Products- AE Intake, Processing & Review, Rev:24 (Effective date: 09/28/15)**

  This SOP **(EXHIBIT 3)** describes the procedure to record and manage AEs for approved drug and biological products and prescription drug products. During the inspection, we reviewed the SOP; no deficiencies were noted.

- **SOP 01-PR-015 Literature Searches and Case Processing Rev:14 (Effective date: 09/28/15)**

  This SOP **(EXHIBIT 4)** describes the procedure for conducting searches of scientific literature to identify reportable adverse events. During the review, we noticed that the firm lacked any mentioning of literature case follow-up process in the SOP. The SOP is currently being revised to reflect case follow-ups for literature cases. A draft copy of the revised version (01-PR-015) is presented as (**EXHIBIT 5).**

- **SOP 01-PR-008 Processing Product Complaint Cases Rev. 14 (Effective date: 09/28/15)**

  This SOP **(EXHIBIT 6)** describes the procedures to document, assess, and act on product complaints for clients who subscribe to the service. During the inspection, we reviewed the SOP; no deficiencies were noted.

- **SOP 01-PR-005 Processing Medical Information Inquiries Rev:19 (Effective date: 10/08/2015)**

  This SOP **(EXHIBIT 7)** describes the procedures for documenting, triaging, and responding to medical information from consumers, healthcare professionals and students. During the inspection we reviewed the SOP; no deficiencies were noted.

15-Day Alert Report

TFB

I, CSO Bernard, reviewed the following 15-Day Reports per the CDER Assignment Memo.

Product	MCM Number	Manufacturer Received Date	FDA Received Date **on Assignment**	Due Date	(b) (4) Ship date	# of Days Late
Nevirapine	2013P1021603	11/25/2013	12/30/2013	12/10/2013	12/05/2013	0
Levetiractam	2015PRN00008	02/25/2015	03/24/2015	03/12/2015	03/20/2015	7
Donepezil	2015PRN00009	02/23/2015	03/24/2015	03/10/2015	03/20/2015	9
Levetiractam	2015PRN00017	04/08/2015	05/27/2015	04/23/2015	04/21/2015	0

Ropinirole Hydrochloride	2015PRN00012	04/14/2015	07/24/2015	04/29/2015	04/29/2015	0

Review of the above 15-Day Alert Cases stated as late were indeed submitted on time to the Agency with the exception to the following cases: case 2015PRN00008 (Levetiractam) and 2015PRN00009 (Donepezil) .

Levetiractam Case # 2015PRN00008, is in reference to a literature report from United States involving a serious and unexpected adverse event of levetiractam. This case is regarding a patient who was being treated with levetiractam and experienced delirium as a side effect. The authors reported that the treating physician in this case documented delirium to be a side effect of the treatment with levetiractam. This case was retrived by (b) (4) on 02/25/2015 and was sent to Prinston on 03/06/2015 for review. The MedWatch 3500A form was not submitted to the Agency until 03/20/2015, which resulted in a 7 days delay **(EXHIBIT 8)**. According to Dr.Tong, Senior Director of Regulatory Affairs, she stated that the reason for the delay was due to them receiving the Medwatch form on a Friday from (b) (4) which led to miscalculation of the due date by a week **(EXHIBIT 9 pg. 2).**

Donepezil Case # 2015PRN00009, is in reference to a literature report form Greece involving a serious and unexpected adverse event of donepezil. This case was regarding an unspecified "overdosing and myoclonus" side effects in a patient with Alzheimer's disease. The author reported that this was the first case of donepezil induced myoclonus caused by overdosing in a patient. This case was retrieved by (b) (4) on 02/23/2015 and was sent to Prinston on 03/06/2015 for review. The case was not submitted until 03/20/2015, which resulted in 9 days delay in submission to the Agency **(EXHIBIT 10).** According to Dr. Tong, they usually receive the MedWatch form on Thursday or Friday from (b) (4) which leaves them 2 or three days after the weekend submission. Dr. Tong stated that the due date was miscalculated by the week **(EXHIBIT 9 pg. 2).**

Nevirapine Case # 2013P1021603, a review of this case revealed that the case was submitted within the required 15 day time frame to the agency. The case was retrieved by (b) (4) on 11/25/2013 and was submitted to Prinston on 12/05/2013 indicated on the Medwatch Report **(EXHIBIT 11 pg.3)**. I requested a copy of the (b) (4) tracking slip to indicate the actual delivery day to the Agency. According to Dr. Tong, they were unable to find the (b) (4) tracking information through (b) (4) current database since the shipment was more than one and a half years ago. She provided documentation of the (b) (4) Billing Online summary **(EXHIBIT 12)**, which reflects the same tracking number #(b) (4) , date: 12/05/2015 indicated on the (b) (4) package slip with the "(b) (4) Overnight" next business day box selected **(Exhibit 11 pg. 1)**.

Levetiractam Case # 2015PRN00017, a review of this case revealed that the case was submitted within the required 15 day time frame to the Agency. The case was retrieved by (b) (4) on 04/08/2015 and was submitted to Prinston on 04/17/2015 indicated on the Initial MedWatch Report **(EXHIBIT 13 pg. 3)** and submission to the Agency on 04/21/2015, which is indicated on the (b) (4) receipt **(EXHIBIT 13 pg. 1)**. According to Dr. Tong, she received correspondence from the Agency on 05/19/2015 indicating that the firm incorrectly submitted the Individual Safety Report, which stated that the report was not submitted on the mandatory reporting 3500 form **(EXHIBIT 14)**. She stated that two copies are always sent to the Agency when submitting the Medwatch forms**.** On 05/22/2015, the 15-Day Alert case was resubmitted **(EXHIBIT 15 pgs. 3 & 4)** and received by the Agency on 05/27/2015 **(EXHIBIT 15 pgs. 1 & 2).**

Ropinirole Case # 2015PRN00012, a review of this case revealed that the case was submitted within the required 15 day time frame. This case is in reference to a spontaneous report received from a health professional via FDA, regarding a patient being treated with Ropinirole HCL tablets and experiencing poor quality of sleep. On 04/14/2015, additional information received from a health professional resulted in the case being reassessed and reported as serious/unexpected. The case was retrieved by (b) (4) on 04/14/2015 and was submitted to Prinston on 04/24/2015. This was indicated on the initial MedWatch Report **(EXHIBIT 16 pg. 4)** and submission to the Agency on 04/29/2015 was also indicated on the (b) (4) receipt **(EXHIBIT 16 pgs. 1&2).** The follow- up report was received on 07/15/2015 and submitted to the Agency on 07/24/2015 via Electronic Gateway Submission **(EXHIBIT 17 pg. 1).**

Select 15-Day Reports (01/01/2013-12/31/2015)

On, 03/30/2016, I CSO Bernard reviewed Prinston Pharmaceutical listing of all expedited cases from January 2013 to December 2015 **(EXHIBIT 18 pg.15)**. According to Dr. Tong, there were no expedited 15 Day Alert late cases for Methocarbamol 500mg, 750mg ANDA 0869889 and ANDA 086988 and Irbesartan/ Hydrochloridthiazide 12.5mg/150mg, 12.5/300mg ANDA 203072 tablets due to no literature findings and no spontaneous findings. The chart listed below are additional 15 day late cases that I CSO Bernard reviewed during the inspection.

Product	ANDA	MCM Number	Aware date	Due Date	(b) (4) Ship date	# of Days Late
Levetiracetam	078106	2014PRN00018	08/04/2014	08/19/2014	08/20/2014	1
Levetiractam	078106	2014PRN00019	08/04/2014	08/19/2014	08/20/2015	1
Levetiractam	078106	2015PRN00056	07/27/2015	08/11/2015	08/13/2015	2
Ropinirole	078110	2015PRN00059	07/27/2015	08/11/2015	08/13/2015	2
Lisinopril	76164	2015PRN00024	04/27/2015	05/12/2015	06/17/2015	35

Levetiracetam Case# 2014PRN000018, is in reference to a literature report from Turkey involving a serious and unexpected adverse event of levetiractam. This case is regarding a patient who was being treated with levetiractam and experienced mycosis fungoides. The authors reported in the case that mycosis fungoides is a reaction when taking levetiractam. The initial case was retrieved by (b) (4) on 08/04/2014 and was sent to Prinston on 08/12/2014 for review and submission to the agency. The MedWatch 3500A form was not submitted until 08/20/2014, which resulted in a 1 day delay in submission to the Agency **(EXHIBIT 19)**. The follow up case revealed that the case was retrieved by (b) (4) on 12/01/2014 and was sent to Prinston on 12/10/2014 and submitted to the Agency on 12/15/2015 **(EXHIBIT 20).** According to Dr.Tong, Senior Director of Regulatory Affairs the reason for the delay was because there was significant new data found in the full text article, so a follow up MedWatch report had to be completed (**EXHIBIT 20 pgs. 9- 13)**.

Levetiracetam Case # 2014PRN000019, is in reference to a literature report from Serbia involving a serious and unexpected adverse event of levetriractam. This case is regarding a child who experienced severe bradycardia. The author reported in the case that servere bradycardia was caused by taking levetriractam. The case was retrieved by (b) (4) on 08/04/2014 and was sent to Prinston on 08/12/2014 and submitted to the Agency on 08/20/2014 **(EXHIBIT 21)**.

Levetiracetam Case # 2015PRN00056, is in reference to a literature report from Turkey involving a serious and unexpected adverse event of levetiracetam. This case is regarding a patient who experienced induced hyponatremia. The author stated that this case demonstrates a rare case of levetiracetam hyponatremia. The case was retrieved by (b) (4) on 07/27/2015 and the MedWatch report was not submitted until 08/13/2015 via E2b, which resulted in a 2 day delay **(EXHIBIT 22).**

Ropinirole Case # 2015PRN00059, is in reference to a literature report from Italy involving a serious and unexpected adverse event of Ripinirole. This case is regarding a patient who experienced dropped head syndrome (DHS). The case was retrieved by (b) (4) on 07/27/2015 and the Medwatch report was not submitted until 08/13/2015 via E2B, which resulted in a 2 day delay **(EXHIBIT 23).**

Lisinipril Case #2015PRN00024, is in reference to a literature report from the United States, involving a serious and unexpected adverse event of Lisinopril. A review of this case revealed that this case was 35 days late due to (b) (4) **(EXHIBIT 24)**. The firm is responsible for collecting and assessing AEs, and submitting the report to Prinston within ten business days. According to the memo provided by (b) (4) they identified the late case and stated that the case will be under quality review. I requested to review the completed deviation /CAPA report from (b) (4) associated with this case **(EXHIBIT 25).** According to the CAPA, the literature AE case was set up

properly. During the case assessment and during the expedited QC, the product was re-selected. That erased the auto-scheduled report, causing it not to show on the expedited list after going through the medical review**.** The case was initially retrieved on 04/27/2015 by (b) (4) and Prinston Pharmaceutical and submitted it to the Agency on 06/17/2015 **(EXHIBIT 26)**.

ICSR Reviews and Periodic Safety Reports (EXHIBIT 46)

ZIG/TFB

During the inspection, we reviewed serious labeled, non-serious labeled and non-serious unlabeled cases that were compiled into quarterly and annual reports. These cases were reviewed against the source documentation and product labeling for seriousness and lateness. The individual cases that we reviewed were Donepezil HCL (Case # 2014PRN00034, Case #20150002), Paroxetine (Case #2015PRN00141) and Benazepril HCL (Case # 2014PRN00026, Case# 2014PRN00027). According to Dr.Tong, Prinston Pharmaceutical is responsible for the preparation and submission of the Periodic Safety Reports to the Agency. All the reports contained the required information, which included: the cover letter addressed to FDA generated by the firm, the name of the drug product the NDA number, the covered reporting period, the number of serious labeled and non-serious labeled reports submitted to the Agency.

Quarterly Reports

- Irbesartan-HCTZ (11/09/2014-02/08/2015): Submitted 03/03/2015
  (02/09/20105-05/08/2015): Submitted 05/22/2015
  (05/09/2015-08/08/2015) Submitted:09/08/2015
  (08/09/2015-11/08/2015) Submitted: 12/03/2015
  (11/09/2015-02/08/2016) Submitted: 03/01/2016
- Paroxetine (10/31/2014-01/30/2015): Submitted03/03/2015
  (01/31/2015-04/30/2015): Submitted:05/19/2015
  (05/01/2015-07/30/2015) : Submitted:08/28/2015
  (07/31/2015-10/30/2015): Submitted:11/25/2015
  (10/31/2015-01/30/2016):Submitted:03/01/2016
- Levetiracetam ER(05/21/2015-08/20/2015): Submitted:09/11/2015

(08/21/2015-11/20/2015): Submitted: 12/03/2015

(11/21/2015-02/200/2016):Submitted:03/18/2016

- Bupropion SR (05/27/2015-08/20/2015): Submitted: 09/111/2015

  (08/21/2015-11/20/2015): Submitted: 12/03/2015

- Valsartan (06/09/2015-09/08/2015): Submitted: 09/11/2015

  (09/09/2015-12/08/2015): Submitted: 12/18/2015

- Escitalopram (08/28/2015-11/27/2015): Submitted 12/03/2015

  (11/28/20115-02/27/2016)Submitted 03/24/2016

Annual Reports

On 4/04/2016 – 4/05/2016, I, CSO Ganiyu reviewed the following Annual PSURs. I did not note any deficiencies. All the reports reviewed were submitted in a timely manner to the Agency. A few reports were submitted near the 60th day deadline, but received on time by the Agency. According to the "Client Protocol" between (b) (4) and Prinston Pharmaceutical **(EXHIBIT 27, pg. 5**), Prinston would receive processed annual reports from (b) (4) within (b) (4) calendar days, which gives Prinston approximately (b) (4) days to complete the report and submit to the Agency.

The Annual PSURs I reviewed on 4/04/2016 – 4/05/2016 were:

- Benazepril HCl (02/11/2014 - 02/10/2015): Submitted 03/11/2015
- Donepezil HCl (05/31/2014 – 05/30/2015): Submitted 07/23/2015**
- Levetiracetam (02/10/2014 – 02/09/2015): Submitted 03/10/2015
- Lisinopril/High Dose (07/01/2014 – 06/30/2015): Submitted 08/28/2015
- Losartan Potassium (06/06/2014 – 06/05/2015): Submitted 08/04/2015*
- Methocarbamol (10/29/2014 – 10/28/2015): Submitted 11/13/2015
- Risperidone (11/29/2014 – 11/28/2015): Submitted 01/08/2016**
- Ropinirole HCl (07/11/2014 – 07/10/2015): Submitted 09/03/2015
- Ropinirole HCl (07/11/2013 – 07/10/2014): Submitted 08/12/2014

*This is the first Annual PSUR of Losartan after last quarterly report of 03/06/2014-6/05/2014.

**This is the first Annual PSUR of Donepezil and Risperidone HCl after quarterly report submissions.

Prinston Pharmaceuticals Standard Operating Procedures (SOPs)

TFB

Prinston Pharmaceutical maintains the following Adverse Events SOPs:

- **PRN-3004.01: Postmarketing Managing and Reporting of Adverse Drug Experience (ADE) effective:10-14-2015**

This SOP **(EXHIBIT 28)** describes the firm's activities regarding adverse events and information inquires received on the marketed generic drug products under Prinston owernership. During the inspection, we noticed that the firm lacked any mentioning of the electronic submission process in the SOP. The SOP is currently being revised to reflect electronic submission. A draft is provided as **(EXHIBIT 29)**

- **PRN-3002.02: Customer Complaint's Drug Product's Quality Compliant effective date: 08/12/2015**

This SOP describes activities regarding product quality complaints received on Prinston Products. During this inspection we reviewed the SOP; no deficiencies were noted.

- **PRN-3003.02: External Audits effective date:03/18/2015**

This SOP describes procedures for conducting audits at vendors/ contract facilities that provide services to Prinston Pharmaceuticals. During the inspection, Ms. Remonda Gergis, Quality Assurance Director stated that (b) (4) was audited on 09/16/2014 to assess their pharmacovigilance services at their drug site in (b) (4) and there were no observations to report.

- **PRN-6003.00 Regulatory Affairs Documentation Control effective date:02/29/2012**

This SOP describes the procedures of receiving, approving, distributing and archiving data and documents received by the Regulatory and Scientific Affairs department for the Agency's submission. During the inspection we reviewed this SOP and no deficiencies were noted.

Electronic Reporting Process

TFB

Prinston currently has an established electronic account for E2B submission in XML format via Electronic Submission Gateway. According to Dr. Tong, Senior Director of Regulatory Affairs the firm has been using the electronic submission gateway system since 06/2015. On 04/04/16, Dr. Tong provided us with Valsartan, Lisinopril, Methocarbamol and Paroxetine PSURs that were submitted electronically. We verified the Agency's acknowledgement of receipt and they were all submitted in a timely manner. Examples of the electronic submissions are provided as **(EXHIBITS 30-33)**. During the review of the firm's SOP# PRN -3004.01: Postmarketing Managing and Reporting of Adverse Drug Experience (ADE) effective: 10-14-2015 **(EXHIBIT 28)**, I noted that the SOP lacked an electronic submission procedural process. I brought this to the attention of Dr. Tong, who agreed and promised to update the SOP. A draft revision of SOP # PRN-3004.02 **(EXHIBIT 29)** was provided to us on 03/30/2016, which reflects e-submission through ESG. An e-submission guide is available to Prinston's ADE submission team if needed **(EXHIBIT 34)**

Adverse Reaction Information System

Prinston's CRO, (b) (4) ((b) (4) uses (b) (4) for adverse events processing. The system was last validated in May 2014 as per memo (**EXHIBIT 35)**.

Inactivated Cases

TFB

According to Dr. Tong, cases would be classified inactivated for the following reasons: duplicate case, non-company product, no identifiable ADE action and no identifiable patient. On 04/01/2016, I reviewed the following cases and reasons they were classified as inactive. The following cases were inactivated: 2015 PRN 00067 (no identifiable adverse drug reaction); 2015PRN00050 (non-company product), 2015PRN00132 (non- company product) and 0015PRN00095 (duplicated case). No deficiencies were noted.

FOLLOW-UPS

ZIG

According to the "Client Protocol" agreement between (b) (4) and Prinston Pharmaceutical, an adverse event follow up is conducted by (b) (4) If follow-up is received, the case

undergoes a case review to determine if changes in the initial assessment are required based on new information received. Please refer to General Discussions with Management for details on follow-up cases.

LITERATURE SEARCHES

ZIG

Literature searches are conducted (b) (4) by (b) (4) in accordance with SOP 01-PR-015, Literature Searches and Case Processing. Searches are based on Prinston's marketed drug products with focus on serious and unexpected adverse event. A review of the SOP revealed no deficiencies.

WAIVER/CLINICAL TRIALS

ZIG

On 3/29/2016, Dr. Tong stated that Prinston Pharmaceutical has no waivers for any of its marketed drug products. She also stated that none of the firm's drugs are currently involved in any clinical trials that Prinston has knowledge of.

Partnership Agreements and Contracts
TFB

I requested all of the safety agreements that Prinston has with their marketing partners. Mr. Hai Wang provided us with the following agreements and contracts. No deficiencies were noted during review.

(b) (4) (formerly (b) (4))

Prinston entered an agreement with (b) (4) on 06/01/2014, which explains pharmacovigilance responsibilities between Prinston and (b) (4) surveys, receives, and medically evaluate ADE cases on behalf of Prinston. Prinston reviews, approves and submits the reports to the Agency **(EXHBIT 36).**

(b) (4)

This is an agreement between (b) (4) and Huandai US/ Prinston which explains the license and supply distribution between the firms. Huandai / Prinston is responsible for the manufacture, testing and release of finished drug product to (b) (4), who distributes products within the USA.

Please Note: (b) (4) currently goes by the name (b) (4) , **(EXHIBIT 37).**

Zhejiang Huhai Pharmaceuticals

This is a quality agreement which outlines responsibilities between Zhejiang Huhai (Manufacturer) and Prinston as the ANDA holder and marketer within the US **(EXHIBIT 38).**

Rising Pharmaceuticals Inc.

This is quality agreement between Rising and Prinston. Rising is responsible for collecting ADEs and Prinston is responsible for submitting them. Rising currently markets one Prinston drug product, which is Losartan HCL **(EXHIBIT 39).**

(b) (4) .

This Safety Data Exchange Agreement between (b) (4) and Huahai US, Inc was terminated on 06/04/2015 **(EXHIBIT 40).**

(b) (4)

The Safety Data Exchange Agreement between (b) (4) and Huahai US, Inc was terminated on 10/03/2014 **(EXHIBIT 41).**

Breckinridge Pharmaceutical, Inc

The Safety Data Exchange Agreement between Prinston and Breckinridge states that Prinston is responsible for manufacturing and Breckinridge is responsible for sale and distribution of Neveripine **(EXHIBIT 42).**

Solco Healthcare US, LLC

This agreement states that Prinston Pharmaceutcal is the owner of the company since 03/13/2012 **(EXHIBIT 43)**

MANUFACTURING CODES
On 3/30/2016, Dr. Tong provided us an email message from (b) (4) describing how Adverse Drug Event (ADE) cases are assigned. According to the email message, ADE cases are assigned as follows:

(b) (4) **AERS** (Effective 6/26/10 to 5/30/14) case numbers were formatted as: **YYYYP1NNNNNN (2013P1004494).**

Code	Represents
YYYY (2013)	Year

P1	(b) (4) (b) (4)
NNNNNN (004494)	(b) (4)

(b) (4) (Effective 5/30/14 – Present) case numbers are formatted as: **YYYYCCCNNNNN (2015PRN00162).**

Code	Represents
YYYY (2015)	Year
CCC (PRN)	(b) (4)
NNNNNN (00162)	(b) (4)

According to the (b) (4) email, the year automatically changes to the next sequential year and the (b) (4) (For example: 2016PRN00001).
We did not note any deficiencies with the manufacturing code during the inspection.

COMPLAINTS
TFB
On 04/04/2016, I reviewed the firm's complaint procedure, which is outlined in Prinston Pharmaceuticals SOP#: PRN-3002.02 "Customer Complaints Drug Product's Quality Complaint" (Effective Date: 04/12/2015). I reviewed complaint logs from January 2015-February 2016 for all Prinston Pharmaceutical products. During the review of the complaint logs, I noticed that there were no complaints that contained ADE information that should have been processed as a MedWatch report. However there were general complaints in reference to odor and other cosmetic related issues. No deficiencies were noted during the review of Prinston Pharmaceutical complaint documentation.

RECALL PROCEDURES
TFB
On 04/01/2016, I reviewed the firms Product Recall Procedure which is outlined in Prinston Pharmaceutical's SOP#: PRN-3005.02 "Product Recall" (Effective Date: 09/09/2015). According to Dr. Tong, there has been no product recall since the establishment of the firm. No deficiencies were noted.

OBJECTIONABLE CONDITIONS AND MANAGEMENT'S RESPONSE

Observations listed on form FDA 483

We did not observe any deficiencies that warranted an insurance of FDA483, Inspectional Observations, during the inspection.

REFUSALS
No refusals were encountered.

GENERAL DISCUSSION WITH MANAGEMENT

ZIG/TFB

On 04/05/2016, a close out meeting was held with the firm's management and the following personnel were present: Jun Du; CEO Hai Wang, Senior Vice President; Wei (Helena) Tong, Senior Director of Regulatory Affairs; Remonda Geris, Senior Director of Quality Affairs; and (b) (6) (b) (6) Regulatory Affairs Associate. No FDA 483, Inspectional Observation was issued. The following two discussion items were verbally discussed:

Updated Client Protocol, Hours of Operation

ZIG

During the current PADE inspection, I inquired about (b) (4) hours of operation. Dr. Tong stated that the hours of operation are covered under "Client Protocol" agreement dated: 02/29/2016 **(EXHIBIT 27, Section 3.1)**. While reviewing the Client Protocol, I noted hours of operation listed as (b) (4) US time. The protocol did not indicate how calls received after (b) (4) are processed. I asked Dr. Tong about ADE reporting coverage after business hours. She stated that ADE phone calls received after operational hours are forwarded to (b) (4) voicemail. On 04/05/2016, the Client Protocol was revised to reflect how outside of business hours calls are forwarded to a voice messaging service and the hours of operation was revised to (b) (4) **(EXHIBIT 44, Section 3.1)**.

Late 15- Day Cases

TFB

During the current inspection, I reviewed Prinston Pharmaceuticals Listing of All Expedited Cases from January 2013 to December 2015 **(EXHIBIT 18)**. A review of the excel sheet provided by Dr. Tong revealed that the firm had a total of 7 late cases which include the two late cases mentioned on page 8 of this report and five cases mentioned on page 10 of this report. These cases were serious unexpected domestic and foreign literature reports. These cases were late for numerous reasons stated earlier in the report. When I brought this to the attention of Dr. Tong, Senior Regualtory Affaris Director, she stated that she had realized the issue and have made the following improvements: to submit all ICSR received during the given week on (b) (4), will contact (b) (4) to discuss whether they can provide ICSR earlier for serious cases such as death, and closely monitor the e-submission and ESG records to ensure that the Agency has acknowledged the submission. The improvements were already implemented as of February 2016 **(Exhibit 9 pg. 2)**.

ADDITIONAL INFORMATION
Dr. Tang provided us a list of (b) (4) drugs that have Pending Approval **(EXHIBIT 45)**

SAMPLES COLLECTED
We did not collect any samples during this inspection.

VOLUNTARY CORRECTIONS
TFB

There were no voluntary corrections to report during the current inspection.

ATTACHMENTS
1(TFB) FDA-482, Notice Of Inspection, , 3 pages
2(TFB) Assignment Memo: Prinston Pharmaceuticals Inc, FY' 16 PADE Inspection, 6 pages

EXHIBITS COLLECTED
1(TFB) Prinston Oral Drug Product List and ADE Responsibilities, 2 pages

2(TFB) Prinston Organizational Chart, 1 page
3(TFB) SOP 01-PR-006 NDA, ANDA BLA DESI, Marketed Health Products and Medicinal Products, 7 pages
4(TFB) SOP 01-PR-015 Literature Searches and Case Processing, 5 pages
5(TFB) SOP 01-PR-015 Literature Searches and Case Processing (DRAFT Revisions), 6 pages
6(TFB) SOP 01-PR-008 Processing Product Complaint Cases, 5 pages
7(TFB) SOP 01-PR-005 Processing Medical Information Inquiries, 8 pages
8(TFB) Levetiractam Case # 2015PRN00008, 9 pages
9(TFB) Justification for late cases 2015PRN0008 & 2015 PRN0009, 2 pages
10(TFB) Donepezil Case# 2015PRN00009, 9 pages
11(TFB) Nevirapine Case # 2013P1021603, 4 pages
12(TFB) (b) (4) Billing Online Summary for Case 2013P1021603, 1 page
13(TFB) Levetiractam Case # 2015PRN00017, 7 pages
14(TFB) Correspondence between Agency and Prinston, 2 pages
15(TFB) Case # 2015PRN00017 Resubmission, 7 pages
16(TFB) Ropinirole Case # 2015 PRN00012- Inital Case, 6 pages
17(TFB) Ropinirole Case # 2015PRN00012- Follow Up, 23 pages
18(TFB) Listing of All Expedited Cases, 15 pages
19(TFB) Levetiracetam Case # 2014PRN00018- Initial, 8 pages
20(TFB) Levetiracetam Case # 2014PRN00018- follow-up, 13 pages
21(TFB) Levetiracetam Case # 2014PRN00019- pdf.pdf, 6 pages
22(TFB) Levetiracetam Case # 2015PRN00056, 19 pages
23(TFB) Ropinirole Case # 2015PRN0059, 19 pages
24(TFB) Memo: Justification for late case#2015PRN00024, 1 page
25(TFB) Deviation and Capa Report for Case#2015PRN00024, 6 pages
26(TFB) Lisinopril Case# 2015PRN00024, 22 pages
27(TFB) (b) (4) and Prinston Client Protocol, 10 pages
28(TFB) SOP PRN-3004.01 Postmarketing Managing And Reporting ADE, 9 pages
29(TFB) SOP PRN-3004.02 Postmarketing Managing and ADE (DRAFT Revision), 10 pages
30(TFB) Electronic Example Valsartan PSUR, 7 pages
31(TFB) Electronic Submission Example 2 Lisinopril, 19 pages
32(TFB) Electronic Submission Example 3 Methocarbamol, 7 pages
33(TFB) Electronic Submission Example 4 Paroxetine, 7 pages
34(TFB) Job Aid for e-submission of ADEs in Prinston, 6 pages
35(TFB) (b) (4) (b) (4) Validation Memo., 1 page
36(TFB) Quality Agreement between Prinston and (b) (4) 13 pages
37(TFB) Agreement between (b) (4) / Huahi/Prinston, 24 pages
38(TFB) Quality agreement between Prinston and Zhejiang Huahai, 38 pages
39(TFB) Quality agreement between Prinston and Rising, 10 pages
40(TFB) Termination of Manufacturing & supply agreement between (b) (4) and Huahai, 3 pages
41(TFB) Memo Termination agreement between Prinston and (b) (4), 1 page
42(TFB) Agreement between Prinston and Breckinridge, 21 pages

43(TFB) Ownership agreement of Solco, 4 pages
44(TFB) (b) (4) and Prinston Client Protocol (REVISED), 10 pages
45(TFB) Prinston Pending Approval ANDA List, 2 pages
46(TFB) Prinston PSUR Report., 7 pages

5/2/2016

X Tonia F Bernard

Tonia F Bernard
Investigator
Signed by: Tonia Bernard -S

5/2/2016

X Zakaria I Ganiyu

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